Case Series

Hemoadsorption (CytoSorb®) in the Management of Septic Shock : our Experience from North East India

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CytoSorb® is a Hemoadsoption device that helps in reduction of cytokines that mediate Sepsis. We present three cases of CytoSorb® therapy in sepsis.

Case 1 : A 43-year-old male presented Septic Shock due to Pneumonia with Acute Respiratory Distress Syndrome, Acute Kidney Injury and was on high dose of vasopressor. His condition progressed to Multiorgan Dysfunction syndrome.

Case 2 : A 69-year-old hypertensive woman presented with sepsis due to complicated urinary tract infection complicated by Acute Kidney Injury, Hepatic Dysfunction and Hyperinflammatory state.

Case 3 : A 70-year-old man diagnosed case of Chronic Kidney Disease and Chronic Airway Diseases presented with Sepsis because of Pneumonia. His condition progressed to Shock requiring high dose of noradrenaline and acute Respiratory Distress Syndrome.

All the three patients required Mechanical ventilation and Dialysis beyond the standard care for Sepsis. CytoSorb® therapy was performed for 1-2 session.

Results : Rapid stabilization of hemodynamics with improvement in sepsis markers were prominent findings. Improvements were observed in SOFA score, conscious level and ventilatory support. Patient of case 1 survived while case 2 & 3 expired.

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Key words **: Septic Shock, CytoSorb®, Hemoadsorption.**

Sepsis is defined as life-threatening organ dysfunction caused by a dysregulated host response to infection and its most severe state, Septic Shock, represents a highly lethal condition that causes substantial morbidity and mortality among critically ill patients[1]. If not managed properly, Sepsis can result in Septic Shock, systemic hyper inflammation and multiple organ failure[2]. Host response to sepsis activates inflammatory response which leads to dysregulation of inflammatory homeostasis with increased levels of both proinflammatory [interleukin (IL)-1β and Tumor Necrosis Factor (TNF) α] and anti-inflammatory (IL-6, IL-8, IL-10) plasma mediators[2]. These mediators (cytokines) lead to responses like hypotension and multiple organ failure. Removal of these cytokines through blood purification therapy may attenuate these responses particularly in the early phase of Sepsis[3].

CytoSorb® is an European CE mark approved and ISO certified hemoadsorption device which helps in reduction of excess inflammatory cytokines in the blood[4].

In previous studies, CytoSorb® therapy has shown clinical benefits if used early (<24 hours) in patients with Septic Shock[5,6]. Here, we present 3 cases of CytoSorb® therapy in severe Sepsis to share our experience.

Editor's Comment :

- CytoSorb® therapy in combination of standard care stabilizes hemodynamics and control of hyperinflammatory response.
- It may be used as bridge therapy in septic shock.

Case 1

A 43-year-old man was admitted at Intensive Care Unit (ICU) on 14.7.2019 (Day 0) with Breathlessness, Cough and Fever for 7 days and reduced urine output for 2 days. He had history of hypertension and drinking ethanol. He was diagnosed as Acute Kidney Injury (AKI) and Acute Respiratory Distress Syndrome (ARDS) secondary to Sepsis because of pneumonia.

At admission :

The patient was tachypneic (Respiratory rate24/min), tachycardic and hemodynamically unstable requiring high doses of noradrenaline(0.20mcg/kg/min) to maintain adequate Mean Arterial Pressure (MAP). He was put on mechanical ventilation because of deteriorating sensorium (GCS 6/15) and development of hypoxemia and ARDS. Antibiotic regimen was Meropenem and levofloxacin. Subsequently, he had multiple organ injury (SGOT-298U/L, SGPT-105U/L, Serum Bilirubin 1.2mg/dl, Serum Amylase 723U/L, Lipase 4409U/L, Lactate

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Dehydrogenase 1442U/L, Creatinine 18.7mg/dl, Urea-209mg/dl) and highly elevated markers for Sepsis (Total leukocyte count-23000/µl with Neutrophils of 95%, C-Reactive Protein (CRP)-296mg/dl, Procalcitonin-30.5mg/dl). Sequential Organ Failure Assessment (SOFA) score was 15 and Serum Lactate level was 3.0mml/L.

His condition deteriorated with higher requirement (0.4mcg/kg/min) of Noradrenaline and additional vasopressin on Day1. Sustained Low Efficiency Dialysis (SLED) was done on Day 1 for severe AKI with metabolic acidosis.

CytoSorb® therapy was done on Day 2 and Day 4. Each treatment was performed with a 4008S machine (Fresenius Medical Care) with treatment duration of 8-10 hours, Blood flow rate 100ml/min, Anticoagulation-low dose heparin.

Changes with CytoSorb® therapy (Table 1) :

Hemodynamic stabilization with improvement in lung function, acidosis, sepsis markers and multi-organ function. Vasopressin infusion was stopped on Day 3 and Noradrenaline infusion was reduced by 50% on Day 3 and stopped on Day 5.

Patient Follow-Up :

Extubating was possible Day 6 but reintubated on day 7 due to refractory hypoxemia and hypercapnia because of Influenza (H1N1). The patient was transferred to normal ward on day 11 and discharged on day 13.

Case 2

A 69-year-old female presented on 1.8.2019 (Day 0) with breathlessness and altered speech for 2 days. She was bedridden at home and had accidental fall twice prior to admission. She had multiple co-morbidities e.g. Hypertension, obstructive sleep apnea, morbid obesity, Coronary Artery Disease (CAD), Chronic Kidney Disease (CKD), lumbar canal stenosis with cauda equina syndrome and chronic bronchial asthma. No history of diabetes. Clinical evaluation and investigations revealed complicated urinary tract infection, acute on chronic kidney disease and sepsis.

At admission :

She had AKI (Serum creatinine 3.99mg/dl, urea 78mg/dl) and liver dysfunction (total Bilirubin 3.3mg/dl, SGOT64U/L, SGPT 48U/L). She was put on mechanical ventilation because of her deteriorated (GCS 4/15) conscious level. There was sudden drop in Blood Pressure (SBP by 30 mm of Hg). She received intermittent SLED and antibiotic therapy with meropenem which was escalated to tigecycline on day 7. Laboratory parameters revealed severe hyperinflammatory state (CRP 284mg/l, procalcitonin>200ng/ml, TLC 29900/µl). SOFA score was 14.

CytoSorb® therapy was done on Day3 and Day5 for 10 hours for each session. Blood flow rate was 100ml/min with 4008s (Fresenius medical care) machine.

Results of CytoSorb® therapy (Table 1) :

Improvement on hemodynamic parameters, conscious level and Sepsis markers but there was dialysis associated hypotension requiring temporary noradrenaline support.

Follow-up :

Though the patient showed improvement after CytoSorb® therapy but not sustained. Total Leukocyte count was increasing from day 8. Her Blood Pressure was not recordable with maximum dose of noradrenaline and vasopressin on day 10 and finally succumbed to death on day10.

Case 3

A 70-Year-old man presented on 3.1.2020 (Day 0) with complain of Fever, increased urinary frequency, reduced urine output and hematuria for 6 days and cough with dyspnea for one day. He had multiple co-morbidities eg, Hypertension, CAD, CKD, Chronic obstructive airway disease and smoking. He was provisionally diagnosed as sepsis because of pneumonia with AKI. Antibiotic therapy with Meropenem and clarithromycin was initiated as per hospital protocol.

After 8 hours of admission, he was drowsy and hemodynamically unstable (BP-90/50 mm of Hg with Noradrenaline 0.2mcg/kg/min). He was intubated and put on Mechanical ventilation due to hypoxemia with ARDS. Laboratory parameters suggested severe hyper-inflammatory state (TLC-27000/µl, CRP-280mg/dl, Procalcitonin 27.7mg/dl).

SOFA Score was 16. SLED was done on Day1 in view of AKI (Creatinine 3.7mg/dl, Urea 204mg/dl) with metabolic acidosis.

CytoSorb® therapy was done on Day3 for 10 hours with blood flow rate of 120ml/min with 4008S machine (Fresenius Medical Care) with low dose heparin.

Results of CytoSorb® therapy (Table 1) :

Hemodynamic stabilization with reduction of noradrenaline dose and improvement of conscious level, ventilatory support and inflammatory markers.

Follow-up :

Patient party counselled for 2nd CytoSorb® therapy but they refused. His condition deteriorated from day 8. Tracheal aspirate culture showed multi-drug resistant klebsiela pneumoniae. His leukocyte counts were rising rapidly. He became hemodynamically unstable and finally succumbed on Day 15.

Discussion

The above three cases showed hemodynamic stabilization with reduction of vasopressor and control of hyperinflammatory state with CytoSorb® therapy in severe Septic Shock. Studies[6,7] have observed the hemodynamic stabilization with improvement of MAP with CytoSorb® therapy which is consistent with our cases. Besides, CytoSorb® therapy showed better clinical outcomes in

laboratory and vital parameters, Sepsis scores, cytokine levels and vasopressor needs[7]. Out of 3 patients, two expired and one survived. Multiple co-morbidities were present in two cases that expired. Although there was transient improvement of these two cases after CytoSorb® therapy, but later on condition deteriorated. Infection with multidrug resistant organism was behind the deterioration. In case 3, only one session of CytoSorb® therapy was feasible due to financial constrain. In the first case infection was controlled with appropriate antibiotic and the clinical response with CytoSorb® therapy was persistent which was not seen in rest two cases. These cases highlight that CytoSorb® therapy may provide bridge therapy till definite control of infection.

Table 1 — *Results of CytoSorb® therapy in 3 cases*

Changes with CytoSorb® therapy	Case 1		Case2		Case3	
Hemodynamic stabilization	Pre-Cytosorb	Post-Cytosorb	Pre-Cytosorb	Post-Cytosorb	Pre-Cytosorb	Post-Cytosorb
MAP	62	90	76	96	63	83
Noradrenaline dose	0.4	0	0	0	0.2	0
Ventilation	VC	Weaning	VC	CPAP-PS	VC	CPAP PS
PaO2/FiO2	135	180	-	-	167	248
GCS	3/15	10/15	2/10	6/10	8/15	11/5
SOFA Score	15	7	14	11	16	10
CRP	296	151	284	55	280	66
Procalcitonin	30	3.87	>200	21.8	25.3	8.01
TLC	24300	11000	29900	40400	22300	35200
Serum creatinine	18.7	3.7	3.99	3.7	3.7	3.7
Urine output	90	1200	350	150	50	125
Patients outcome	Survived		Expired		Expired	

Note : Post-Cytosorb means 24-hour after last CytoSorb® therapy, VC-Volume Control, CPAP-PS: Continuous Positive Airway Pressure-pressure Support, MAP-mean Arterial Pressure, GCS-Glasgow Coma Scale, Sofa-sequential Organ Failure Assessment, CRP-C-Reactive Protein, TLC-Total Leukocyte Count

It has been shown[5,6] that CytoSorb® therapy if initiated in early Septic Shock (within 24 hours of onset) give better clinical benefits. We performed CytoSorb® at 48 hours for Case 1 & 3 and 72 hours for Case 2. In Case 2, there was drop of Blood pressure more than 30% but was above the target MAP (65 mm of Hg) prior to CytoSorb®.

Late initiation of CytoSorb® may be another reason for poor response. Mehta, *et al*[7] developed scoring system for initiation of CytoSorb® therapy in Septic Shock patient that might help in selecting patients.

Conclusion

In patients with Sepsis due to infection, CytoSorb® in the combination with standard therapy resulted in rapid stabilization of hemodynamics and control of hyperinflammatory response. CytoSorb® is safe and easy to administer and advantageous extracorporeal therapy for Sepsis with multiorgan dysfunction syndrome in the sense that it provides bridge therapy by controlling the inflammatory response till the definite cure.

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